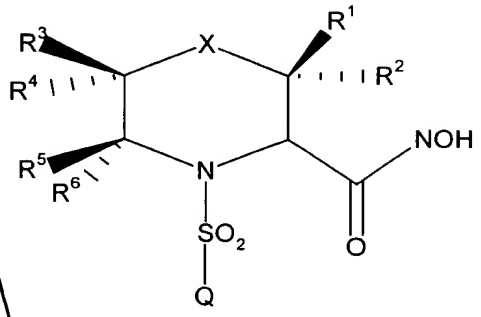
CLAIMS

1. A compound of the formula



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or the pharmaceutically acceptable salt thereof, wherein

X is oxygen, sulfur, SO, SO_2 or NR^7;

R^1, R^2, R^3, R^4, R^5 and R^6 are selected from the group consisting of hydrogen, hydroxy, NH_2, -CN, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_6-C_{10})aryl(C_2-C_6)alkenyl, (C_2-C_9)heteroaryl(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_6-C_{10})aryl(C_2-C_6)alkynyl, (C_2-C_9)heteroaryl(C_2-C_6)alkynyl, (C_1-C_6)alkylamino, $[(C_1-C_6)alkyl]_2$amino, (C_1-C_6)alkylthio, (C_1-C_6)alkoxy, perfluoro(C_1-C_6)alkyl, perfluoro(C_1-C_6)alkoxy, (C_6-C_{10})aryl, (C_2-C_9)heteroaryl, (C_6-C_{10})arylamino, (C_6-C_{10})arylthio, (C_6-C_{10})aryloxy, (C_2-C_9)heteroarylamino, (C_2-C_9)heteroarylthio, (C_2-C_9)heteroaryloxy, (C_3-C_6)cycloalkyl, (C_1-C_6)alkyl(hydroxymethylene), piperidyl, (C_1-C_6)alkylpiperidyl, (C_1-C_6)acyl, (C_1-C_6)acylamino, (C_1-C_6)acylthio, (C_1-C_6)acyloxy, (C_1-C_6)alkoxy-(C=O)-, $-CO_2H$, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, and $[(C_1-C_6)alky]_2$-N-(C=O)-;

wherein said (C_1-C_6)alkyl is optionally substituted by one or two groups selected from (C_1-C_6)alkylthio, (C_1-C_6)alkoxy, trifluoromethyl, halo, -CN, (C_6-C_{10})aryl, (C_2-C_9)heteroaryl, (C_6-C_{10})arylamino, (C_6-C_{10})arylthio, (C_6-C_{10})aryloxy, (C_2-C_9)heteroarylamino, (C_2-C_9)heteroarylthio, (C_2-C_9)heteroaryloxy, (C_6-C_{10})aryl(C_6-C_{10})aryl, (C_3-C_6)cycloalkyl, hydroxy, piperazinyl, (C_6-C_{10})aryl(C_1-C_6)alkoxy, (C_2-C_9)heteroaryl(C_1-C_6)alkoxy, (C_1-C_6)acylamino, (C_1-C_6)acylthio, (C_1-C_6)acyloxy, (C_1-C_6)alkylsulfinyl, (C_6-C_{10})arylsulfinyl, (C_1-C_6)alkylsulfonyl, (C_6-C_{10})arylsulfonyl, amino, (C_1-C_6)alkylamino or $((C_1-C_6)alkyl)_2$amino;

R^7 is hydrogen; (C_1-C_6)alkyl optionally substituted by one or more of hydroxy, -CN, (C_1-C_6)alkylamino, (C_1-C_6)alkylthio, (C_1-C_6)alkoxy, perfluoro(C_1-C_6)alkyl, (C_6-C_{10})aryl, (C_6-C_{10})arylthio, (C_6-C_{10})aryloxy, (C_2-C_9)heteroarylamino, (C_3-C_6)cycloalkyl, (C_1-C_6)alkyl(hydroxymethylene), piperidyl, (C_1-C_6)alkylpiperidyl, (C_1-C_6)acyl, (C_1-C_6)acylamino, (C_1-C_6)acyloxy, (C_1-C_6)alkoxy-(C=O)-, $-CO_2H$, (C_1-C_6)alkyl-NH-(C=O)-, and $[(C_1-C_6)alky]_2$-N-(C=O)-; (C_6-C_{10})arylsulfonyl; (C_1-C_6)alkylsulfonyl; (C_1-C_6)alkyl-NH-(C=O)-; (C_1-C_6)alkoxy-

(C=O)-; (C_1-C_6)alkyl-(C=O)-; [(C_1-C_6)alky]$_2$-N-(C=O)-; or (R^8R^9N)-(C=O) where R^8 and R^9 are taken together with the nitrogen that they are attached to form a ring selected from azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl and thiomorphonyl;

Q is (C_6-C_{10})aryl(C_1-C_6)alkoxy(C_6-C_{10})aryl, (C_6-C_{10})aryl(C_1-C_6)alkoxy(C_2-C_9)heteroaryl, (C_2-C_9)heteroaryl(C_1-C_6)alkoxy(C_6-C_{10})aryl, or (C_2-C_9)heteroaryl(C_1-C_6)alkoxyC_2-C_9)heteroaryl, wherein each of said (C_6-C_{10})aryl or (C_2-C_9)heteroaryl groups may optionally be substituted by one or more substituents, preferably one to three substituents per ring, most preferably one to three substituents on the terminal ring independently selected from the group consisting of halo, -CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms, (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH-, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, (C_1-C_6)alkyl-SO_2-[N-(C_1-C_6)alkyl]-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, phenyl(C_1-C_6)alkyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl;

with the provisio that when X is SO or SO_2, and R^3 and R^4 are a substituent comprising a heteroatom, the heteroatom cannot be bonded to the ring;

and with the proviso that at least one of R^1-R^6 must be (C_1-C_6)alkyl;

and with the proviso that when X is oxygen or sulfur and R^3-R^6 are each hydrogen then R^1 and R^2 cannot both be methyl.

2. A compound according to claim 1, wherein X is >NR^7, sulfur or oxygen.

3. A compound according to claim 1, wherein Q is (C_6-C_{10})aryl(C_1-C_6)alkoxy(C_6-C_{10})aryl, (C_6-C_{10})aryl(C_1-C_6)alkoxy(C_2-C_9)heteroaryl, (C_2-C_9)heteroaryl(C_1-C_6)alkoxy(C_6-C_{10})aryl or (C_2-C_9)heteroaryl(C_1-C_6)alkoxy(C_2-C_9)heteroaryl optionally substituted by one or more, preferably one to three substituents per ring, most preferably one to three substituents on the terminal ring, wherein said substituent is selected from halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or perfluoro(C_1-C_3)alkyl.

4. A compound according to claim 1, wherein Q is (C_6-C_{10})arylmethoxy(C_6-C_{10})aryl, (C_6-C_{10})arylmethoxy(C_2-C_9)heteroaryl, (C_2-C_9)heteroarylmethoxy(C_6-C_{10})aryl or (C_2-

C_9)heteroarylmethoxy(C_2-C_9)heteroaryl optionally substituted by one or more, preferably one to three substituents per ring, most preferably one to three substituents on the terminal ring, wherein said substituent is selected from halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or perfluoro(C_1-C_3)alkyl.

5. A compound according to claim 1, wherein Q is optionally substituted (C_6-C_{10})arylmethoxyphenyl, pyridylmethoxyphenyl, furylmethoxyphenyl, pyroylmethoxyphenyl, thienylmethoxyphenyl, isothiazolylmethoxyphenyl, imidazolylmethoxyphenyl, benzimidazolylmethoxyphenyl, tetrazolylmethoxyphenyl, pyrazinylmethoxyphenyl, pyrimidylmethoxyphenyl, quinolylmethoxyphenyl, isoquinolylmethoxyphenyl, benzofurylmethoxyphenyl, isobenzofurylmethoxyphenyl, benzothienylmethoxyphenyl, pyrazolylmethoxyphenyl, indolylmethoxyphenyl, isoindolylmethoxyphenyl, purinylmethoxyphenyl, carbazolylmethoxyphenyl, isoxazolylmethoxyphenyl, thiazolylmethoxyphenyl, oxazolylmethoxyphenyl, benzthiazolylmethoxyphenyl, benzoxazolylmethoxyphenyl.

6. A compound according to claim 1, wherein Q is (C_6-C_{10})arylmethoxy(C_6)aryl optionally substituted by one or more, preferably one to three substituents per ring, most preferably one to three substituents on the terminal ring, wherein said substituents are independently selected from halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or perfluoro(C_1-C_3)alkyl.

7. A compound according to claim 1, wherein Q is (C_6-C_{10})arylmethoxy(C_2-C_9)heteroaryl optionally substituted by one or more, preferably one to three substituents per ring, most preferably one to three substituents on the terminal ring, wherein said substituents are independently selected from halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or perfluoro(C_1-C_3)alkyl.

8. A compound according to claim 1, wherein Q is (C_2-C_9)heteroarylmethoxy(C_6)aryl optionally substituted by one or more, preferably one to three substituents per ring, most preferably one to three substituents on the terminal ring, wherein said substituents are independently selected from halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or perfluoro(C_1-C_3)alkyl.

9. A compound according to claim 1, wherein Q is (C_2-C_9)heteroarylmethoxy(C_2-C_9)heteroaryl optionally substituted by one or more, preferably one to three substituents per ring, most preferably one to three substituents on the terminal ring, wherein said substituents are independently selected from halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or perfluoro(C_1-C_3)alkyl.

10. A compound according to claim 1, wherein R^4 is hydrogen.

11. A compound according to claim 1, wherein R^2 or R^3 are hydrogen.

12. A compound according to claim 1, wherein at least one of R^2 or R^3 is other than hydrogen.

13. A compound according to claim 1, wherein at least one of R^1-R^3 is (C_1-C_6)alkyl.

14. A compound according to claim 2, wherein at least one of R^1-R^3 is (C_1-C_6)alkyl.

15. A compound according to claim 3, wherein at least one of R^1-R^3 is (C_1-C_6)alkyl.

16. A compound according to claim 1, wherein at least one of R^1-R^3 is methyl.

17. A compound according to claim 2, wherein at least one of R^1-R^3 is methyl.

18. A compound according to claim 3, wherein at least one of R^1-R^3 is methyl.

19. A compound according to claim 3, wherein R^1 is (C_1-C_6)alkyl.

20. A compound according to claim 3, wherein R^2 is (C_1-C_6)alkyl.

21. A compound according to claim 3, wherein R^3 is (C_1-C_6)alkyl.

22. A compound according to claim 3, wherein R^4 is (C_1-C_6)alkyl.

23. A compound according to claim 1 wherein R^1 and R^4 are each methyl.

24. A compound according to claim 2 wherein R^1 and R^4 are each methyl.

25. A compound according to claim 3 wherein R^1 and R^4 are each methyl.

26. A compound according to claim 1, wherein R^1 and R^2 are each (C_1-C_6)alkyl.

27. A compound according to claim 2, wherein R^1 and R^2 are each (C_1-C_6)alkyl.

28. A compound according to claim 3, wherein R^1 and R^2 are each (C_1-C_6)alkyl.

29. A compound according to claim 1, wherein R^1 and R^2 are each methyl.

30. A compound according to claim 2, wherein R^1 and R^2 are each methyl.

31. A compound according to claim 3, wherein R^1 and R^2 are each methyl.

32. A compound according to claim 1 wherein R^1 is methyl and R^2 is hydrogen;

33. A compound according to claim 1 wherein R^1 is hydrogen and R^3 is methyl.

34. A compound according to claim 3, wherein R^1 and R^3 are each methyl.

35. A compound according to claim 3, wherein R^1 and R^4 are each methyl.

36. A compound according to claim 3, wherein R^2 and R^3 are each methyl.

37. A compound according to claim 3, wherein R^2 and R^4 are each methyl.

38. A compound according to claim 3, wherein R^3 and R^4 are each methyl.

39. A compound according to claim 1 wherein X is NR^7.

40. A compound according to claim 3 wherein X is NR^7.

41. A compound according to claim 4 wherein X is NR^7.

42. A compound according to claim 5 wherein X is NR^7.

43. A compound according to claim 6 wherein X is NR^7.

44. A compound according to claim 13 wherein X is NR^7.

45. A compound according to claim 15 wherein X is NR^7.

46. A compound according to claim 1 wherein X is NR^7 and R^7 is $(C_1\text{-}C_6)$alkyl.

47. A compound according to claim 1 wherein X is NR^7 and R^7 is $(C_1\text{-}C_6)$alkylsulfonyl.

48. A compound according to claim 1 wherein X is NR^7 and R^7 is $(C_6\text{-}C_{10})$arylsulfonyl.

49. A compound according to claim 1 wherein X is NR^7 and R^7 is $[(C_1\text{-}C_6)\text{alkyl}]_2N\text{-}(C{=}O)\text{-}$ or $(C_1\text{-}C_6)\text{alkylNH-}(C{=}O)\text{-}$.

50. A compound according to claim 1 wherein X is NR^7 and R^7 is $(C_1\text{-}C_6)\text{alkyl}(C{=}O)\text{-}$.

51. A compound according to claim 1, wherein said compound is selected from the group consisting of:

(2*S*,3*S*)-4-[4-(3,5-difluro-benzyloxy)-benzenesulfonyl]-2-methyl-thiomorpholine-3-carboxylic acid hydroxyamide;

(2S,3S)-4-[4-(4-fluoro-benzyloxy)-benzensulfonyl]-2-methyl-thiomorpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-2,6-dimethyl-4-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

4-(4-benzyloxy-benzenesulfonyl)-2-methyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(3*R*,6*S*)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-2,2,6-trimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-6-ethyl-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-2-methyl-morpholine-3-carboxylic acid hydroxyamide;

(2*R*,3*R*,6*S*)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*R*,3*R*,6*R*)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-2,6-dimethyl-4-[4-(pyridin-4-ylmethoxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-2,6-dimethyl-4-[4-(pyridin-2-ylmethoxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-2,6-dimethyl-4-[4-(pyridin-3-ylmethoxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-2,6-dimethyl-4-[4-(2-methyl-pyridin-3-ylmethoxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(3*R*,6*S*)-2,2,6-trimethyl-4-[4-(2-trifluoromethyl-benzyloxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*)-2,6,6-trimethyl-4-[4-(pyridin-4-ylmethoxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(3*R*,6*S*)-2,2,6-trimethyl-4-[4-(2-methyl-pyridin-3-ylmethoxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-[4-(2,5-dimethyl-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-4-[4-(3,5-difluoro-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-4-[4-(3-methoxy-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-4-[4-(5-fluoro-2-methyl-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-4-[4-(furan-3-ylmethoxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-4-[4-(2-fluoro-3-methyl-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-2,6,6-trimethyl-morpholine-3-carboxylic acid hydroxyamide;

(*3R*)-*4*-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-6,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(*3R*)-*6*,6-dimethyl-4-[4-(pyridin-4-ylmethoxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(*3R*)-*6*,6-dimethyl-4-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-4-(4-cyclohexylmethoxy-benzenesulfonyl)-2,6-dimethyl-morpholine-3-carboxylic acid hydroxyamide;

(*3R,6S*)-*4*-[4-(2,5-dimethyl-benzyloxy)-benzenesulfonyl]-2,2,6-trimethyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-6-methoxymethyl-2-methyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*S*)-4-[4-(3-chloro-benzyloxy)-benzenesulfonyl]-6-[(ethyl-methyl-amino)-methyl]-2-methyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*)-4-[4-(3-chloro-benzyloxy)-benzenesulfonyl]-6-methoxy-2-methyl-morpholine-3-carboxylic acid hydroxyamide;

(2*S*,3*R*,6*R*)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-6-hydroxymethyl-2-methyl-morpholine-3-carboxylic acid hydroxyamide.

52. A pharmaceutical composition for the treatment of a condition which can be treated by the inhibition of a matrix metalloproteinase in a mammal, including a human, comprising an amount of a compound of claim 1 effective in such treatment and a pharmaceutically acceptable carrier.

53. A pharmaceutical composition for the treatment of a condition which can be treated by the inhibition of a mammalian reprolysin in a mammal, including a human, comprising an amount of a compound of claim 1 effective in such treatment and a pharmaceutically acceptable carrier.

54. A pharmaceutical composition for the treatment of arthritis, inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity, cachexia, allergic reactions, allergic contact hypersensitivity, cancer, tissue ulceration, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joint implants, atherosclerosis, aortic aneurysm, congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neuro-degenerative disorders, autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neuropathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, diabetes, tumor invasion, tumor growth, tumor metastasis, corneal scarring, scleritis, AIDS, sepsis and septic shock in a mammal, including a human, comprising an amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof, effective in such treatments or inhibition and a pharmaceutically acceptable carrier.

55. A method for the inhibition of the the cellular production/release of tumor necrosis factor (TNF) in a mammal, including a human, comprising administering to said mammal an effective amount of a compound of claim 1.

56. A method for treating a condition selected from the group consisting of arthritis, inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity, cachexia, allergic reactions, allergic contact hypersensitivity, cancer, tissue ulceration, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joint implants, atherosclerosis, aortic aneurysm, congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neuro-degenerative disorders, autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neuropathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, diabetes, tumor invasion, tumor growth, tumor metastasis, corneal scarring, scleritis, AIDS, sepsis and septic shock in a mammal, including a human, comprising administering to said mammal an amount of a compound of claim 1, effective in treating such a condition.

57. A method of inhibiting the cleavage of TNF-α from cell membranes in a mammal comprising administering to such mammal an effective amount of compound according to claim 1 that inhibits the TNF-α proteolytic activity of TACE.

58. A method of inhibiting TNF-α cleavage from cell membranes comprising blocking the binding of TNF-α to TACE with a compound of claim 1.

59. A method for treating a mammal having a disease characterized by an unregulated cellular production/release of TNF-α, comprising administering to the mammal a composition comprising an amount of a compound according to claim 1 that effectively inhibits the TNF-α proteolytic activity of TACE.

60. A method of inhibiting the cleavage of TNF-α from cell membranes without inhibiting MMP-1 in a mammal, comprising administering to such mammal an effective amount of a small molecule that inhibits the TNF-α proteolytic activity of TACE without inhibiting MMP-1.

61. A method of inhibiting the cleavage of TNF-α from cell membranes without inhibiting MMP-1 in a mammal comprising administering to such mammal an effective amount of a hydroxamic acid compound that inhibits the TNF-α proteolytic activity of TACE without inhibiting MMP-1.

62. A method for treating a mammal having a disease characterized by an overproduction of soluble TNF-α, comprising administering to the mammal a composition

comprising an amount of a small molecule that effectively inhibits the proteolytic activity of TACE on membrane bound TNF-α, without inhibiting MMP-1.

63. A method of inhibiting the cleavage of TNF-α from cell membranes and inhibiting MMP-13 selectively over MMP-1 in a mammal comprising administering to such mammal an effective amount of an agent that inhibits the TNF-α proteolytic activity of TACE and inhibits MMP-13 selectively over MMP-1.

64. A method of inhibiting the cleavage of TNF-α from cell membranes and inhibiting MMP-13 selectively over MMP-1 in a mammal comprising administering to such mammal an effective amount of a hydroxamic acid compound that inhibits the TNF-α proteolytic activity of TACE and inhibits MMP-13 selectively over MMP-1.

65. A method for treating a mammal having a disease characterized by an overproduction of soluble TNF-α, comprising administering to the mammal a composition comprising an amount of a small molecule that effectively inhibits the proteolytic activity of TACE on membrane bound TNF-α and inhibits Aggrecanase, without inhibiting MMP-1.

66. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of an agent that selectively inhibits the TNF-α proteolytic activity of TACE in preference to MMP-1.

67. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of a hydroxamic acid compound , wherein said hydroxamic acid compound selectively inhibits the TNF-α proteolytic activity of TACE in preference to MMP-1.

68. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of an agent, wherein said agent inhibits the TNF-α proteolytic activity of TACE and inhibits MMP-13 selectively over MMP-1 .

69. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of a hydroxamic acid compound, wherein said hydroxamic acid compound inhibits the TNF-α proteolytic activity of TACE and inhibits MMP-13 selectively over MMP-1 .

70. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of an Aggrecanase inhibitor, wherein said Aggrecanase inhibitor selectively inhibits Aggrecanase in preference to MMP-1.

71. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of an Aggrecanase inhibitor, wherein said Aggrecanase inhibitor selectively inhibits Aggrecanase at least ten times as well as MMP-1.

72. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of an Aggrecanase inhibitor, wherein said Aggrecanase inhibitor selectively inhibits Aggrecanase and MMP-13 in preference to MMP-1.

73. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of an Aggrecanase inhibitor, wherein said Aggrecanase inhibitor selectively inhibits Aggrecanase and MMP-13 at least ten times as well as MMP-1.

74. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of a hydroxamic acid Aggrecanase inhibitor, wherein said hydroxamic acid Aggrecanase inhibitor selectively inhibits Aggrecanase and MMP-13 in preference to MMP-1.

75. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of a hydroxamic acid Aggrecanase inhibitor, wherein said hydroxamic acid Aggrecanase inhibitor selectively inhibits Aggrecanase and MMP-13 at least ten times as well as MMP-1.

76. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of an agent, wherein said agent selectively inhibits Aggrecanase and TACE in preference to MMP-1.

77. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of a hydroxamic acid, wherein said hydroxamic acid selectively inhibits Aggrecanase and TACE at least ten times as well as MMP-1.

78. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of an agent, wherein said agent selectively inhibits Aggrecanase, MMP-13 and TACE in preference to MMP-1.

79. A method of treating arthritis in a mammal, comprising administering to such mammal an effective amount of a hydroxamic acid, wherein said hydroxamic acid selectively inhibits Aggrecanase, MMP-13 and TACE at least ten times as well as MMP-1

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